

REMARKS

Claims 7-8, 16-18

Claims 7-8 and 16-18 have been rejected under 35 USC 102(b) as being anticipated by Branton et al. (WO 00/079257) as evidenced by Stryer (citation in office action).

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Moreover, the identical invention must be shown in as complete detail as contained in the claim. *Richardson v. Suzuki Motor Co.* 868 F.2d 1226, 1236, 9USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants respectfully assert that the rejection of claim 7 is improper.

Regarding claim 7, the rejection indicates that [p]olymerases are proteins, which comprise chemical functional groups.” Applicants respectfully challenge this assertion on several grounds.

First, it appears that the Examiner is stating that Branton inherently discloses functional groups by disclosing use of a polymerase, which may be a protein, which may be based on an amino acid with a functional group, because the rejection states that Stryer has been added merely for the teaching that proteins comprise functional groups and the claims remain rejected over the prior art of record. Particularly, it appears that the Examiner is asserting that polymerases are proteins, and then by extension that proteins in general have functional groups because they include amino acids, which may have functional groups.

However, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). Rather, to establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may

result from a given set of circumstances is not sufficient.’ *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted). In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.” *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

To support the Examiner’s position that Branton inherently discloses the claimed chemical functional groups, Stryer has been cited to purportedly show that polymerases are proteins. Particularly, the Examiner cites p. 575 of Stryer, noting that “Stryer explicitly states ...that DNA polymerases are protein.” However, a review of Stryer p. 575 failed to disclose where Stryer explicitly states that a DNA polymerase is a protein. Therefore, the rejection fails to include a proper basis in fact as required by *Ex parte Levy, supra*.

Moreover, Stryer does indicate that DNA polymerase 1 is an enzyme, but it is known that not all enzymes are proteins. Therefore, the rejection relies on the *possibility* that Branton’s polymerase is not only the same as that in Stryer, but also that Stryer’s DNA polymerase is a protein, and yet further that the protein is formed of amino acids that may have functional groups, and further that, after all the processing necessary to convert the amino acids to the DNA polymerase, what were the functional groups in the starting material are still functional groups rather than nonfunctional. As can be seen, the logic of the rejection relies on too many levels of possibilities to support the Examiner’s assertion of inherency. Again, “[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *In re Robertson, supra*.

For any of the foregoing reasons, the rejection of claim 1 is improper.

Claims 8 and 16-18 depend from claim 7, and therefore incorporate the limitations of claim 7. By virtue of their dependence, claims 8 and 16-18 are also believed to be allowable.

Claims 1-5, 12-15

Claims 1-5 and 12-15 have been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger (J. Polymer Sci. Part A; Poly. Chem., vol. 37, pp.2685-2698 (1999)) as evidenced by Stryer.

Applicants assert that the rejection is improper as failing the *Graham* test. The analysis of obviousness was set forth in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966). In order to establish a *prima facie* case of obviousness, three basic criteria must be met:

First, there must be some *suggestion or motivation*, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the teachings of the references. Second, there must be a *reasonable expectation of success*. Finally, the prior art reference or combined references must teach or suggest *all the claim limitations*. *The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art*, and not based on applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991; *emphasis added*)).

Applicants respectfully traverse the rejection as failing the *Graham* test. Specifically, the combination proposed in the rejection fails at least the first element of the *Graham* test.

First, the claimed invention would not have been predictable from the bare teachings of the prior art itself, or in knowledge generally known to those skilled in the art. The United States Supreme Court has acknowledged that there is no obviousness where the end result is unpredictable. In the recent case, *KSR International v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), the Court's analysis included by implication the traditional notion that evidence of unpredictable results is evidence of non-obviousness. Therefore, even though the Court made sweeping changes to the obviousness analysis, it acknowledged that a showing of unpredictable results could defeat an assertion of obviousness.

The courts have repeatedly stated that the chemical arts are, by their very nature, unpredictable. This case is no different. In the instant rejection, the Examiner proposes replacing Branton's polymerase with a cyclic molecule from Hoger. However, no showing has been made that such a substitution would work, and allow Branton's device to continue to operate. Rather,

any result of such a substitution is truly unpredictable. For instance, will Branton's crosslinkers couple to Hoger's cyclical molecule? If so, what will the effect be on the resultant diameter of the cyclical molecule? Will it still allow passage of Branton's single strand of DNA? Further, would Branton's invention even work after such a substitution? (Note Branton's reliance on the "biological motor" created by polymerase and DNA at p. 36, line 23 to p. 38, line 30.)

The lack of any description of using cyclicals in Branton is further evidence that such a substitution was not predictable to those skilled in the art.

Moreover, the Examiner cites Scheme 4 on p. 2689 of Hoger for the proposition that the rings can be coupled to a support. However, as clearly shown on p. 2689 of Hoger and described in the first partial paragraph of col. 1 thereof, Scheme 4 is a synthesis process in which the precursors are attached to the solid support and, upon formation of the ring break free. Assuming the same result in Branton if Hoger's rings were employed therewith, the rings would appear to break free from Branton's aperture.

Further, a reading of the column on p. 2689 of Hoger directly under the drawing labeled "Scheme 4" indicates that the precursors coupled to the solid substrate are found to couple together, voiding the reaction that is to create the ring. Accordingly, whether one of Hoger's rings would form in Branton's aperture, or would couple with another of the precursors, adds yet another layer of unpredictability to the combination proposed by the Examiner.

Because the result of the substitution proffered in the rejection is unpredictable, the claimed invention is not obvious. Accordingly, the rejection is erroneous.

Expanding on the point above, even assuming *arguendo* that substitution of Branton's polymerase with Hoger's cyclic molecule would somehow render predictable results, such results would appear to result in rendering Branton's device inoperable, and thus unsatisfactory for its intended purpose.

Applicants therefore respectfully traverse the rejection of claim 1 as being improper, as the proposed modification would render Branton's invention unsatisfactory for its intended purpose. If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the

proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Particularly, the purpose of Branton's system is to analyze portions of a DNA strand as it moves through a hole. However, if Hoger's cyclical molecule were added as suggested by the Examiner, the DNA strand would couple with the cyclical and stop. Therefore, Branton's device would no longer be able to analyze the strand in the hole, or any other strand in the sample.

Moreover, the Examiner indicates in section F of the Office Action that the Applicant's argument regarding the binding of the Branton's DNA strand to Hoger's cyclical if added to Hoger's aperture undermines Applicant's claim 11. The Examiner is respectfully directed to claim 11, which recites "wherein said aperture is functionalized to bind to a specific biological or chemical moiety". Accordingly, Applicant's arguments do not undermine the embodiment of claim 11. Rather, the binding is an intended function of claim 11. In sharp contrast, such binding would indeed undermine Branton's device which, as set forth by the Examiner in section G of the Office Action, is "for evaluation a polymer molecule by causing the polymer molecule to move through an aperture in sequential order."

Further, Hoger Scheme 4 is relied upon to show that Hoger's cyclical can be coupled to a substrate. However, as noted above, Hoger teaches that neighboring precursors coupled to the solid substrate are found to react with each other together, voiding the reaction that is to create the ring. *See* the column on p. 2689 of Hoger directly under the drawing labeled "Scheme 4".

For any one of the foregoing reasons, Branton's device would be rendered inoperable, in violation of *In re Gordon, supra*.

Accordingly, the rejection is improper for this reason as well.

Also, Hoger appears to teach away from coupling the rings to a solid support. A *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the claimed invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997). Particularly, the rejection relies on Scheme 4 of Hoger. However, a reading of the column on p. 2689 directly under the drawing labeled "Scheme 4" indicates that Scheme 4 is not preferred. Particularly, the author notes that the precursors are found to couple

together, voiding the reaction that is to create the ring. Further, at one point, the author refers to Scheme 4 as requiring “extreme approaches”. *See* Hoger, p. 2689, first column.

Accordingly, because Hoger teaches away from a ring coupled to a solid support, the rejection violates the rule of *In re Geisler, supra*, and must be withdrawn.

Further, the rejection proposed would require an impermissible change in the principle of operation of Branton. Particularly, Branton relies on the “biological motor” created by polymerase and DNA to pull the DNA through the hole. To remove the polymerase and replace it with Hoger’s cyclical would cause the DNA strand to bind up in the hole rather than be drawn through it, thereby defeating the principle of operation of Branton’s critical biological motor. If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Accordingly, the rejection is improper for this reason as well.

For any of the foregoing reasons, reconsideration and allowance of claim 1 is respectfully requested.

Claims 2-5 and 12-15 depend from claim 1, and therefore incorporate the limitations of claim 1. By virtue of their dependence, claims 2-5 and 12-15 are also believed to be allowable. If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Reconsideration and allowance of claims 2-5 and 12-15 is respectfully requested.

Further, the deficiencies of the reliance on Stryer set forth above are incorporated by reference here for those claims for which the rejection relies on Stryer.

Claim 6

Claim 6 has been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Hoger as evidenced by Stryer in yet further view of Go (US5104820).

The rejection of claim 6 applies Branton and Hoger as for claim 1. Claim 6 depends from claim 1, and therefore the rejection suffers from the same deficiencies as set forth above with respect to claim 1. Because Go has merely been added to allegedly show the limitation of the dependent claim, claim 6 is believed to be allowable over the combination proposed by the Examiner. Reconsideration and allowance of claim 6 is respectfully requested.

Claims 7 and 9

Claims 7 and 9 have been rejected under 35 USC 103(a) as being unpatentable over Branton in view of Go.

The rejection of claims 7 and 9 applies Branton as for claim 7, and therefore is erroneous for the same reasons as set forth above, namely that the rejection based on Branton is unsupported and/or improperly relies on official notice.

Reconsideration and allowance of claims 7 and 9 is respectfully requested.

Conclusion

In the event that the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, he or she is respectfully requested to initiate the same with the undersigned at (408) 971-2573.

Respectfully submitted,

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